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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/666,870	09/20/2000	Andrew D. Ellington	119927-1030	8382

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EXAMINER
EPPERSON, JON D

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/11/2003

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
File Copy	09/666,870	ELLINGTON ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-49 and 54-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-49 and 54-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

1. The Response filed May 22, 2003 (Paper No. 20) is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 47-53 were pending in the Application (the Examiner withdrew claims 1-46 from consideration in Paper No. 18). Applicants cancelled claims 1-46 and 50-53 in Paper No. 20 and added claims 54-66. Therefore, claims 47-49 and 54-66 are pending and examined on the merits in this case.

Withdrawn Objections/Rejections

4. All objections to specification are withdrawn in view of Applicants' amendments. The objections to claims 51-53 are withdrawn in view of Applicants' cancellation of said claims. With respect to the rejections under the first paragraph of 35 U.S.C. 112, the rejection encompassing claims 50-53 is withdrawn in view of Applicants' cancellation of said claims. With respect to the rejections under the second paragraph of 35 U.S.C. 112, the rejections denoted A-D are withdrawn in view of applicants' amendments to the claims and/or cancellation of claims. The Marshall et al, Cox et al and Scaringe et al rejection under 35 U.S.C. § 103(a) is hereby withdrawn in view of Applicants' cancellation of claims 50-53. The Hesselberth et al,

Cox et al and Scaringe et al rejection under 35 U.S.C. § 103(a) is hereby withdrawn in view of Applicants' cancellation of claims 50-53. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claims Rejections - 35 U.S.C. 102

5. Claims 47, 49, 54-59 and 61-66 are rejected under 35 U.S.C. 102(a) as being anticipated by Marshall et al (Marshall, K. A.; Ellington, A. D. "Training ribozymes to switch" Nature Structural Biology **November 1999**, 6 (11), 992-4).

For ***claims 47, 59 and 66***, Marshall et al discloses "aptazyme chips" wherein different ribozyme ligases are immobilized on beads in wells to monitor the presence and concentrations of different metabolites or proteins (see Marshall et al, entire document, especially figure 3; see also page 994, last paragraph), which anticipates claims 47, 59 and 66. For example, Marshall et al discloses aptazyme chips for "monitor[ing] the presence and concentrations of different metabolites or proteins" wherein a "ribozyme ligase", which anticipates the preamble of claim 47 because an "aptazyme reaction" is being "detected" when the ribozyme ligase covalently bonds to a reporter in the presence of cognate effectors. Marshall et al also discloses "aptazymes" on a solid support, which reads on lines 2-5 of claim 47 (see Marshall et al, figure 3, "ribozyme ligases ... are shown immobilized on beads in wells ... [o]ne advantage of this scheme is that covalent immobilization of reporters ... should allow extremely stringent wash steps to be

employed"). Marshall et al also discloses "at least one analyte" and "providing substrate tagged to be detectable" in lines 7-8 of claim 47 (see Marshall et al, figure 3, "ribozyme ligases ... immobilized on beads in wells and mixtures of analytes and fluorescently tagged substrates have been added to each well"). Marshall et al also discloses the immobilization of a substrate to the aptazyme upon activation of the aptazyme with an analyte wherein a signal is produced after washing unbound substrate off the substrate (see Marshall et al, figure 3, "after reaction and washing, the presence and amounts of co-immobilized fluorescent tags are indicative of he amounts of ligands that were present during the reaction"). Please also note that Marshall et al discloses applicants preferred embodiment (compare Marshall et al, figure 3 and page 994, last paragraph to applicant's specification, pages 60-61, especially page 60, line 19 which references the Marshall et al paper).

For **claims 49 and 61**, Marshall et al discloses the use of "amplification" for increasing the amount of aptamer or aptazyme with the desired characteristics and thus increase the signal produced (see Marshall et al, figure 1) (see also Marshall, page 994 last paragraph, "Interestingly, aptazyme ligases have the unique property of being able to transduce effectors into templates that can be amplified, affording an additional boost in signal prior to detection"), which anticipates claim 49.

For ***claims 54 and 62***, Marshall et al discloses fluorescently tagged substrates (see Marshall et al, page 993, figure 3).

For ***claims 55-56 and 63-64***, Marshall et al discloses beads in wells on a multiwell plate (see Marshall et al, page 993, figure 3).

For ***claim 57***, Marshall et al discloses different aptazymes immobilized in different wells (see Marshall et al, page 993, figure 3).

For ***claims 58 and 65***, Marshall et al discloses metabolites and proteins (see Marshall et al, page 993, figure 3).

Response

6. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicant argues that that the Marshall reference is unavailable as prior art in the instant application as a result of the Declaration submitted by Dr. Andrew D. Ellington under 35 C.F.R. § 1.131. Here, Applicants argue that the Marshall reference merely "refers to the work that generated the inventions claimed in the instant application [i.e., the work by Ellington, Robertson, Cox and Davidson]" and that "the inventions claimed in the instant application were invented before the publication date of the Marshall reference" (see Paper No. 20, paragraph bridging pages 13-14).

This is not found persuasive for the following reasons:

The Declaration of Prior Invention filed on May 2, 2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the Marshall et al reference. The Examiner contends **[1]** that the Declaration is defective because it does not contain a signature from all of the

inventors as required by MPEP § 715.04. Furthermore, the Examiner contends **[2]** that the evidence submitted is insufficient to establish a reduction to practice of the invention in this country or a NAFTA or WTO member country prior to the effective date of the Marshall et al reference. Applicants have not provided any evidence whatsoever. In addition, the Examiner contends **[3]** that the evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the Marshall et al reference. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897). Here, Applicants have provided no evidence whatsoever. Finally, the Examiner contends **[4]** that the evidence submitted is insufficient to establish diligence from a date prior to the date of reduction to practice of the Marshall et al reference to either a constructive reduction to practice or an actual reduction to practice. Here, Applicants have provided no evidence whatsoever. See also MPEP § 715.07, "The essential thing to be shown under 37 CFR 1.131 is priority of invention and this may be done by any satisfactory evidence of the fact. FACTS, not conclusions, must be alleged. Evidence in the form of exhibits may accompany the affidavit or declaration. Each exhibit relied upon should be specifically referred to in the affidavit or declaration, in terms of what it is relied upon to show."

Accordingly, the 35 U.S.C. 102 rejection cited above is hereby maintained.

7. Claims 47, 49, 54, 58, 61-62 and 65-66 are rejected under 35 U.S.C. 102(a) as being anticipated by Hesselberth et al (Hesselberth, J.; Robertson, M. P.; Jhaveri, S.; Ellington, A. D. "In vitro selection of nucleic acids for diagnostic applications" Reviews in Molecular *Biotechnology* **March 2000**, *74*, 15-25).

For ***claims 47, 59 and 66***, Hesselberth et al discloses methods for the "high-throughput construction of chips to sense proteomes and metabolomes" (see Hesselberth et al, entire document, pages 23-24; section 5), which anticipates claims 47, 59 and 66. For example, Hesselberth et al discloses that "aptazymes" can be "covalently immobilize[d] ... in discrete sectors of arrays" like "chip[s]" (see Hesselberth et al, page 24, last paragraph, "For example, a host of signaling aptamers could be synthesized with terminal amines, immobilized on glass, and an analyte mixture could be applied to the glass surface"). Hesselberth et al also discloses method steps for using the immobilized aptazymes to detect individual analytes by their ability to "pull down" labeled substrates that can then be detected after washing away unbound substrate (see Hesselberth et al, page 24, last paragraph, "The presence of quantities of individual analytes could then be determined by monitoring the changes in fluorescence intensity in individual sectors of the chip. Similarly, aptazymes could be immobilized and analytes and oligonucleotide tags introduced together. Since the pairing between the aptazymes and the oligonucleotide tags can be altered at will, analytes could activate specific aptamers in specific sectors to pull down specific tags. In this way, analyte detection might not only be spatially but also spectrally resolved. Moreover because the tags are covalently

immobilized to the aptazyme, which in turn covalently immobilized to the chip surface, aptazyme chips can be stringently washed to reduce non-specific binding and background").

For ***claims 49 and 61***, Hesselberth et al discloses the ribozymes with appended tags can be "preferentially amplified" (see Hesselberth et al, entire document, especially page 16, paragraph 1), which anticipates claim 49.

For ***claims 54 and 62***, Hesselberth et al discloses fluorescent substrates (see Hesselberth et al, page 24, column 1, last paragraph).

For ***claims 58 and 65***, Hesselberth et al discloses proteins (see Hesselberth et al, page 19, column 1, paragraph 1; see also page 23, column 2, paragraph 2).

Response

8. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicant argues that that the Hesselberth reference is unavailable as prior art in the instant application as a result of the Declaration submitted by Dr. Andrew D. Ellington under 35 C.F.R. § 1.131. Here, Applicants argue that the Hesselberth reference merely "refers to the work that produced the inventions claimed in the instant application [i.e., the work by Ellington,

Robertson, Cox and Davidson]" and that "these inventions were not described in a printed publication before Applicants invented them" (see Paper No. 20, page 15).

This is not found persuasive for the following reasons:

The Declaration of Prior Invention filed on May 2, 2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the Hesselberth et al reference. The Examiner contends **[1]** that the Declaration is defective because it does not contain a signature from all of the inventors as required by MPEP § 715.04. Furthermore, the Examiner contends **[2]** that the evidence submitted is insufficient to establish a reduction to practice of the invention in this country or a NAFTA or WTO member country prior to the effective date of the Hesselberth et al reference. Applicants have not provided any evidence whatsoever. In addition, the Examiner contends **[3]** that the evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the Hesselberth et al reference. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897). Here, Applicants have provided no evidence whatsoever. Finally, the Examiner contends **[4]** that the evidence submitted is insufficient to establish diligence from a date prior to the date of reduction to practice of the Hesselberth et al reference to either a constructive reduction to practice or an actual reduction to practice. Here, Applicants have provided no evidence whatsoever. See also MPEP § 715.07, "The essential thing to be shown under 37 CFR 1.131 is priority of invention and this may be done by any satisfactory evidence of the fact. FACTS, not conclusions, must be

alleged. Evidence in the form of exhibits may accompany the affidavit or declaration. Each exhibit relied upon should be specifically referred to in the affidavit or declaration, in terms of what it is relied upon to show."

Accordingly, the 35 U.S.C. 102 rejection cited above is hereby maintained.

Claims Rejections – 35 U.S.C. 102/103

9. Claims 47-49 and 54-66 are rejected under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Marshall et al (Marshall, K. A.; Ellington, A. D. "Training ribozymes to switch" Nature Structural Biology **November 1999**, 6 (11), 992-4).

For ***claims 47, 59 and 66***, Marshall et al discloses "aptazyme chips" wherein different ribozyme ligases are immobilized on beads in wells to monitor the presence and concentrations of different metabolites or proteins (see Marshall et al, entire document, especially figure 3; see also page 994, last paragraph), which anticipates claims 47, 59 and 66. For example, Marshall et al discloses aptazyme chips for "monitor[ing] the presence and concentrations of different metabolites or proteins" wherein a "ribozyme ligase", which anticipates the preamble of claim 47 because an "aptazyme reaction" is being "detected" when the ribozyme ligase covalently bonds to a reporter in the presence of cognate effectors. Marshall et al also discloses "aptazymes" on a solid support i.e., they are disclosing "apatazyme chips", which reads on lines 2-5 of claim 47 (see

Marshall et al, figure 3, "ribozyme ligases ... are shown immobilized on beads in wells ... [o]ne advantage of this scheme is that covalent immobilization of reporters ... should allow extremely stringent wash steps to be employed"). Marshall et al also discloses "at least one analyte" and "providing substrate tagged to be detectable" in lines 7-8 of claim 47 (see Marshall et al, figure 3, "ribozyme ligases ... immobilized on beads in wells and mixtures of analytes and fluorescently tagged substrates have been added to each well"). Marshall et al also discloses the immobilization of a substrate to the aptazyme upon activation of the aptazyme with an analyte wherein a signal is produced after washing unbound substrate off the substrate (see Marshall et al, figure 3, "after reaction and washing, the presence and amounts of co-immobilized fluorescent tags are indicative of he amounts of ligands that were present during the reaction").

For **claims 48 and 60**, although Marshall et al does not specifically mention the use of "automation" with disclosed methods for using "aptazyme chips", automation would be would be immediately envisaged (e.g., anticipated) or in the alternative prima facie obvious to one of ordinary skill in the art because "chip" are made for automation i.e., they are used and designed for high throughput screening. See *In re Schaumann*, 572 F.2d 312. 197 USPQ 5 (CCPA 1978).

For **claims 49 and 61**, Marshall et al discloses the use of "amplification" for increasing the amount of aptamer or aptazyme with the desired characteristics and thus increase the signal produced (see Marshall et al, figure 1) (see also Marshall, page 994 last paragraph, "Interestingly, aptazyme ligases have the unique property of being able to

transduce effectors into templates that can be amplified, affording an additional boost in signal prior to detection"), which anticipates claim 49.

For ***claims 54 and 62***, Marshall et al discloses fluorescently tagged substrates (see Marshall et al, page 993, figure 3).

For ***claims 55-56 and 63-64***, Marshall et al discloses beads in wells on a multiwell plate (see Marshall et al, page 993, figure 3).

For ***claim 57***, Marshall et al discloses different aptazymes immobilized in different wells (see Marshall et al, page 993, figure 3).

For ***claims 58 and 65***, Marshall et al discloses metabolites and proteins (see Marshall et al, page 993, figure 3).

10. Claims 47-49, 56, 58-62 and 65-66 are rejected under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hesselberth et al (Hesselberth, J.; Robertson, M. P.; Jhaveri, S.; Ellington, A. D. "In vitro selection of nucleic acids for diagnostic applications" Reviews in Molecular Biotechnology March 2000, 74, 15-25).

For ***claims 47, 59 and 66***, Hesselberth et al discloses methods for the "high-throughput construction of chips to sense proteomes and metabolomes" (see Hesselberth et al, entire document, pages 23-24; section 5), which anticipates claim 47. For example, Hesselberth et al discloses that "aptazymes" can be "covalently immobilize[d] ... in discrete sectors of arrays" like "chip[s]" (see Hesselberth et al, page 24, last paragraph, "For example, a host of signaling aptamers could be synthesized with terminal amines,

immobilized on glass, and an analyte mixture could be applied to the glass surface"). Hesselberth et al also discloses method steps for using the immobilized aptazymes to detect individual analytes by their ability to "pull down" labeled substrates that can then be detected after washing away unbound substrate (see Hesselberth et al, page 24, last paragraph, "The presence of quantities of individual analytes could then be determined by monitoring the changes in fluorescence intensity in individual sectors of the chip. Similarly, aptazymes could be immobilized and analytes and oligonucleotide tags introduced together. Since the pairing between the aptazymes and the oligonucleotide tags can be altered at will, analytes could activate specific aptamers in specific sectors to pull down specific tags. In this way, analyte detection might not only be spatially but also spectrally resolved. Moreover because the tags are covalently immobilized to the aptazyme, which in turn covalently immobilized to the chip surface, aptazyme chips can be stringently washed to reduce non-specific binding and background").

For ***claims 48 and 60***, although Hesselberth et al does not specifically mention the use of "automation" with disclosed methods for using the "chips", automation would be would be immediately envisaged (e.g., anticipated) or in the alternative prima facie obvious to one of ordinary skill in the art because "chip" are made for automation i.e., they are used and designed for high throughput screening. See *In re Schaumann*, 572 F.2d 312. 197 USPQ 5 (CCPA 1978).

For ***claims 49 and 61***, Hesselberth et al discloses the ribozymes with appended tags can be "preferentially amplified" (see Hesselberth et al, entire document, especially page 16, paragraph 1), which anticipates claim 49.

For ***claims 54 and 62***, Hesselberth et al discloses fluorescent substrates (see Hesselberth et al, page 24, column 1, last paragraph).

For ***claims 58 and 65***, Hesselberth et al discloses proteins (see Hesselberth et al, page 19, column 1, paragraph 1; see also page 23, column 2, paragraph 2).

Response

11. Applicant's arguments directed to the above 35 U.S.C. § 102/103 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicant argues that the Marshall et al and Hesselberth et al references are not available as prior art under 35 U.S.C. §102 or under 35 U.S.C. § 103 in the instant application as a result of the Declarations set forth by Andrew Ellington.

This is not found persuasive for the following reasons:

The Examiner contends that the Marshall et al and Hesselberth et al references are available under 35 U.S.C. § 102 and § 103 because the Declarations by Andrew Ellington are defective as set forth in the 35 U.S.C. § 102 rejections above (see above 35 U.S.C. § 102(a) rejections which are incorporated in their entirety herein by reference).

Accordingly, the 35 U.S.C. 102/103 rejection cited above is hereby maintained.

Claim Rejections - 35 USC § 103

12. Claims 47-49, 54-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marshall et al (Marshall, K. A.; Ellington, A. D. "Training ribozymes to switch" Nature Structural Biology **November 1999**, 6 (11), 992-4) and Cox et al (Cox, J. C.; Rudolph, P.; Ellington, A. D. "Automated RNA Selection" *Biotechnol. Prog.* **1998**, 14, 845-850).

For **claims 47, 49, 54-59 and 61-66**, Marshall et al teaches all the limitations stated in the 35 U.S.C. 102(a) rejection above (incorporated in its entirety herein by reference), which anticipates claims 47, 49, 54-59, 61-66 and, consequently, also renders obvious claims 47, 49, 54-59, 61-66.

For ***claims 48 and 60***, the prior art teachings of Marshall et al differs from the claimed invention by not specifically reciting the use of a "automation" for the method of detecting an aptazyme reaction. Marshall et al is deficient in that it only teaches the use of "chips", which only implies that automation would be used since chips are designed for large scale automation (see Marshall et al, page 993, figure 3).

However, Cox teaches that in vitro selection can be "automated" (see entire document, especially figure 1).

Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the method of Marshall et al with the "automation" equipment as taught by Cox et al because Cox et al teaches that their automation procedures can be used with aptamers in procedures that involve in vitro selection as required by the method steps

Marshall et al. Furthermore, one of ordinary skill in the art would have been motivated to use a "automation" because Cox explicitly states that "[a]utomated selection can now be used to generate nucleic acid aptamers in days rather than weeks or months" i.e. one of skill in the art would have immediately recognized the time savings that could be obtained through automation and the possibility of increased throughput (see Cox et al, entire document, especially abstract).

Response

13. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicant argues that that the Cox reference is unavailable as prior art in the instant application as a result of the Declaration submitted by Dr. Andrew D. Ellington under 35 C.F.R. § 1.131. Here, Applicants argue that the Cox reference merely "refers to the work that produced the inventions claimed in the instant application [i.e., the work by Ellington, Robertson, Cox and Davidson]" and that "these inventions recited by the instant application were invented before the publication date of the Cox reference" (see Paper No. 20, page 16). Applicant further argues that the Marshall reference is not available.

This is not found persuasive for the following reasons:

The Declaration of Prior Invention filed on May 2, 2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the Cox et al reference. The Examiner contends **[1]** that the Declaration is defective because it does not contain a signature from all of the inventors as required by MPEP § 715.04. Furthermore, the Examiner contends **[2]** that the evidence submitted is insufficient to establish a reduction to practice of the invention in this country or a NAFTA or WTO member country prior to the effective date of the Cox et al reference. Applicants have not provided any evidence whatsoever. In addition, the Examiner contends **[3]** that the evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the Cox et al reference. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897). Here, Applicants have provided no evidence whatsoever. Finally, the Examiner contends **[4]** that the evidence submitted is insufficient to establish diligence from a date prior to the date of reduction to practice of the Cox et al reference to either a constructive reduction to practice or an actual reduction to practice. Here, Applicants have provided no evidence whatsoever. See also MPEP § 715.07, "The essential thing to be shown under 37 CFR 1.131 is priority of invention and this may be done by any satisfactory evidence of the fact. FACTS, not conclusions, must be alleged. Evidence in the form of exhibits may accompany the affidavit or declaration. Each exhibit relied upon should be specifically referred to in the affidavit or declaration, in terms of what it is relied upon to show."

Furthermore, the Examiner contends that the Marshall et al reference is available because the Declaration under 37 C.F.R. § 1.131 by Andrew Ellington is defective (see response to 35 U.S.C. § 102 rejection above regarding the Marshall et al reference, which is incorporated in its entirety herein by reference).

Accordingly, the 35 U.S.C. 103(a) rejection cited above is hereby maintained.

14. Claims 47, 49, 54, 58, 61-62 and 65-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hesselberth et al (Hesselberth, J.; Robertson, M. P.; Jhaveri, S.; Ellington, A. D. "In vitro selection of nucleic acids for diagnostic applications" Reviews in Molecular Biotechnology March 2000, 74, 15-25) and Cox et al (Cox, J. C.; Rudolph, P.; Ellington, A. D. "Automated RNA Selection" Biotechnol. Prog. **1998**, 14, 845-850).

For **claims 47, 49, 54, 58, 61-62 and 65-66**, Hesselberth et al teaches all the limitations stated in the 35 U.S.C. 102(a) rejection above (incorporated in its entirety herein by reference), which anticipates claims 47, 49, 54, 58, 61-62, 65-66 and, consequently, also renders obvious claims 47, 49, 54, 61-62, 65-66.

For ***claims 48 and 60***, the prior art teachings of Hesselberth et al differs from the claimed invention by not specifically reciting the use of a "automation" for the method of detecting an aptazyme reaction. Hesselberth et al is deficient in that it only teaches the use of "chips", which only implies that automation would be used since chips are

designed for large scale automation (see Hesselberth et al, page 24, last paragraph; see also abstract).

However, Cox teaches that in vitro selection can be "automated" (see entire document, especially figure 1).

Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the method of Hesselberth et al with the "automation" equipment as taught by Cox et al because Cox et al teaches that their automation procedures can be used with aptamers in procedures that involve *in vitro* selection as required by the method steps Hesselberth et al. Furthermore, one of ordinary skill in the art would have been motivated to use a "automation" because Cox explicitly states that "[a]utomated selection can now be used to generate nucleic acid aptamers in days rather than weeks or months" i.e. one of skill in the art would have immediately recognized the time savings that could be obtained through automation and the possibility of increased throughput (see Cox et al, entire document, especially abstract).

Response

15. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicant argues that the Cox et al and Hesselberth et al references are not available as prior art under 35 U.S.C. §102 or under 35 U.S.C. § 103 in the instant application as a result of the Declarations set forth by Andrew Ellington.

This is not found persuasive for the following reasons:

The Examiner contends that the Cox et al and Hesselberth et al references are available under 35 U.S.C. § 103 because the Declarations by Andrew Ellington are defective as set forth in the 35 U.S.C. § 102 & 103 rejections above (see above responses to 35 U.S.C. § 102/103 rejections which are incorporated in their entirety herein by reference).

Accordingly, the 35 U.S.C. 103(a) rejection cited above is hereby maintained.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D. Epperson, Ph.D. whose telephone number is (703) 308-2423. The examiner can normally be reached on Monday-Thursday from 9:30 to 7:00 and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jon D. Epperson, Ph.D.
July 31, 2003

BENNETT CELSA
PRIMARY EXAMINER